UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,332	02/13/2006	Gunter Stempfer	BPG-33315A/BCK	6279

72554 7590 11/02/2009

SANDOZ INC
506 CARNEFIE CENTER
PRINCETON, NJ 08540

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
11/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,332	STEMPFER ET AL.	
	Examiner	Art Unit	
	SANDRA WEGERT	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 2, 4-9,12-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-9, 12, 13, 15 and 23* is/are rejected.

7)☒ Claim(s) *14,16-22 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Prosecution on the merits of this application is reopened on claims 1, 2, 4-9 and 12, considered unpatentable for the reasons indicated in the Office Action of 1 May 2009. The finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. The amendment and Remarks, sent 31 July 2009, have been entered into the record. Claims 1, 4 and 12 have been amended. Claims 3, 10 and 11 are cancelled.

Claims 1, 2, 4-9 and 12-24 are under examination in the Instant Application.

Withdrawn Objections and Rejections

35 USC § 112, first paragraph - Written Description.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

The rejection of claims 1 and 7-12, under 35 U.S.C. 112, first paragraph, for lack of Written Description, is *withdrawn*. This rejection was made previously (1 May 2009, pp. 6-8) because the claims recited or embraced use of an "agent" without specifying the chemical structure of the recited "agent." Applicants amended the independent claim to specify the type of agents specified in the specification that are used for performing

osmotic shock (Amended claims, 13 July 2009).

Maintained/New Claim Rejections/Objections

Claim Objections -

Claims 14 and 16-24 are objected to for depending from a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112- second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 13 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is incomplete in that it is not known what a "crude preparation" of recombinant interferon alpha is, nor how it is obtained. For example, there is a series of steps recited in previous claims and in dependent claims such as claim 14 and claim 24 that specify the source of the crude preparation; however, those steps are not recited in claim 13 prior to the steps of refining the crude preparation.

Claim 23 is included in this rejection because it is dependent from the specifically mentioned claims without resolving the indefiniteness issue belonging thereto.

35 USC § 112, first paragraph - Written Description.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 15 is directed to a process for the preparation of a recombinant polypeptide using fermentation methods with prokaryotic host cells, and extraction of the polypeptides by adding an "agent" directly to the fermentation medium. However, the claim does not specify precisely what substances may be used as "agents," nor does it describe the properties that such an "agent" would possess, such that one could recognize whether applicants were in possession of such an agent or class of agents.

The specification teaches adding distilled water, sucrose, or alcohol to disrupt the integrity of the bacterial cell walls in the fermentation medium. However, the specification does not teach functional or structural characteristics of an "agent," other than those listed, to be used for the claimed methods. The description of one or a few agents is not adequate written description of an entire genus of functionally-equivalent molecules that might include many other types of molecules or formulations.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of one functional requirements of the "agent," and one that has not been adequately identified. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the *agents* referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed *agents* and, therefore, would not know how to use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of use. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The agent *itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be

unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, use of only agents that produce an osmotic disruption in the bacterial cell walls, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections- 35 USC § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. 102 that forms the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-9 and 12 are rejected 35 U.S.C. 102(b) as being anticipated by Bochner et al (1987, US Patent 4,680,262). Bochner et al disclose a method for the preparation of growth hormone or any peptide of interest from transformed E. coli cells. The reference describes the process of fermentation as culturing the cells at 37 °C and pH 7.5 for 36 hours, after which steam is immediately injected into the fermenter jacket, the temperature of the tank rises rapidly to 50 °C, and the high temperature is held for 10 minutes (Example 8, column 12). The polypeptides are described as being injected into the *periplasm* of the transformed E. coli host cells (see Title and Abstract) as recited by

the instant independent claims. In addition, the reference discusses extraction of the polypeptide of interest by osmotic *shock* (column 2, line 46), as recited in claims 1 and 2 and encompassed by all claims. In addition, Bochner et al discuss agents used for osmotic shock, such as *sucrose* (column 5, line 32), as well as typical concentrations used for fermentation extraction of proteins, such as 20% sucrose. Terms specific to Claims 7-9 are disclosed throughout the reference: the bacteria are *Gram-negative* (Column 1, line 48); the host cell used was *E. coli* (see Example 1); and the reference discloses a method of producing other polypeptides of interest, such as interferons (top of column 4).

Applicants have argued against Bochner, et al being used as prior art because they contend that Bochner, et al did not apply the osmotic shock to the cells in the fermentation medium and that they did not produce interferon alpha (Remarks, 31 July 2009, p. 7).

Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

Bochner et al (1987, US Patent 4,680,262) contemplates applying osmotic shock directly to the fermentation medium (see column 2, line 45; column 3, second paragraph and column 4, lines 56-58). In addition, Bochner, et al describes the process as useful for producing other mammalian proteins, such as interferons (column 4). Interferons include interferon alpha, an interferon that is not atypical of the genus and is well-described in the literature (http://en.wikipedia.org/wiki/Interferon, accessed 20 October 2009). Thus Bochner, et al anticipates claims 1, 2, 4-9 and 12 in their entirety.

Conclusion:

Claims 1, 2, 4-9, 12, 13, 15 and 23 are rejected for the reasons cited above. Claims 14, 16-22 and 24 are objected to.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Nickol, can be reached at (571) 272-0835.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

/SLW/
20 October 2009

/Dong Jiang/
Primary Examiner, Art Unit 1646